

ULF TYLÉN

Angiography in Inflammatory and Malignant
Diseases of the Pancreas

Lund 1972

ANGIOGRAPHY IN INFLAMMATORY AND MALIGNANT
DISEASES OF THE PANCREAS

Akademisk avhandling

som med vederbörligt tillstånd av Medicinska Fakulteten i Lund för
vinnande av medicine doktorsgraden kommer att offentligen försvaras
i föreläsningssal 3, Centralblocket, Lasarettet i Lund, torsdagen
den 5 oktober 1972 kl. 09.15

av

Ulf Tylén
Med.lic., Klm.



FROM THE DEPARTMENT OF DIAGNOSTIC RADIOLOGY (DIRECTOR: PROFESSOR
OLLE OLSSON), UNIVERSITY HOSPITAL, LUND, SWEDEN.

U L F T Y L É N

ANGIOGRAPHY IN INFLAMMATORY AND MALIGNANT DISEASES OF
THE PANCREAS

Lund 1972

The investigations were supported by grants from the Swedish Medical Research Council No. B71-23X-521-07C, B72-23X-521-08 and B73-14X-521-09.



Printed in Sweden
Studentlitteratur
Lund 1972

This thesis is based on the following papers:

- I. BOIJSEN E. and TYLÉN U.: Vascular changes in chronic pancreatitis. Acta Radiol. Diagnosis 12 (1972), 34.
- II. TYLÉN U. and DENCKER H.: Roentgenologic diagnosis of pancreatic abscess. Acta Radiol. Diagnosis. In press.
- III. TYLÉN U. and ARNESJÖ B.: Angiographic diagnosis of inflammatory disease of the pancreas. Acta Radiol. Diagnosis. In press.
- IV. TYLÉN U.: Angiographic differentiation between inflammatory disease and carcinoma of the pancreas. Acta Radiol. Diagnosis. In press.
- V. TYLÉN U.: The accuracy of angiography in the diagnosis of carcinoma of the pancreas. Accepted by Acta Radiol. Diagnosis.

Introduction

Diseases of the exocrine pancreas are not very common, but the incidence of carcinoma in this gland is increasing (Beall et coll. 1970, Krain 1970, National Board of Health and Welfare. Cancer Incidence in Sweden 1972). It is discouraging to note that the results of surgery in this type of tumour are extremely poor (Beall et coll. 1970, Feduska et coll. 1971, Pope and Fish 1971). This may be due to the localization of the pancreas, making early symptoms uncharacteristic and thereby causing delay in the diagnosis. Moreover, the pancreas is located close to structures of vital importance, such as the superior mesenteric artery and the portal vein. Invasion of these structures often occurs early on rendering radical surgery impossible. The localization also makes the gland inaccessible to diagnosis by inspection or palpation other than at operation. However, a preoperative diagnosis is desirable and should be made early enough to permit successful removal of the tumour.

In order to obtain an early and accurate diagnosis of pancreatic carcinoma a combination of different methods is usually necessary. Many sophisticated methods have been elaborated, such as analysis of the exocrine pancreatic secretion with regard to enzyme content and exfoliated cells (Lundh 1962, Goldstein and Ventzke 1968, Dreiling 1970, Bourke et coll. 1972) and scintigraphy of the pancreas. The results of the latter method are contradictory and the future value of the method is not yet possible to foresee (Desgrez et coll. 1972, Krönert et coll. 1972, McCarty et coll. 1972).

The diagnosis of pancreatic carcinoma by roentgenological methods prior to the time of selective visceral angiography was necessarily based upon indirect evidence i.e. it was not possible to demonstrate the tumour per se, but only involvement of adjacent organs, such as the biliary tract, the stomach or the duodenum by displacement or overgrowth (Rösch 1967). Some investigators have achieved good results in this way (Salik 1961, Perez et coll. 1965) but others have been less successful (Frimann-Dahl 1961). The methods

are generally limited to growths of the head of the pancreas in addition. With the introduction of refined methods such as percutaneous transhepatic cholangiography (Wiechel 1964, Seldinger 1966), hypotonic duodenography (Rubinstein et coll. 1972, Böttger et coll. 1972), retroperitoneal gas insufflation with tomography (Guién et coll. 1970) and splenoportography (Anacker et coll. 1963, Rösch 1965) more tumours are diagnosed, but usually not early enough as all these methods are based on extension of the tumour growth beyond the gland.

Pancreatography, i.e. injection of contrast medium into the ducts of the pancreas, is a method of demonstration of the internal gland but has hitherto been used very little in the diagnosis since it may only be used during operation (Doubilet et coll. 1955, Howard and Short 1969, Trapnell 1971). The advances of endoscopy in recent years, however, has made pancreatography available by means of duodenoscopic cannulation of the papilla of Vater (Oi et coll. 1970, Takagi et coll. 1970, Weiss et coll. 1972). The method, however, demands great skill and experience with endoscopic work and is therefore not yet applicable for routine work.

The advent of selective visceral angiography offered a more direct approach to the internal pancreas by demonstration of involvement of the pancreatic vasculature (Olsson 1970). During the last decade angiography has therefore gained acceptance in the diagnosis of pancreatic disease. However, many authors investigating the value of angiography in pancreatic disease have been discouraged by the difficulty in differentiating carcinoma of the pancreas from inflammatory disease. This particular problem is also common to other diagnostic methods and may also be present at operation even with the aid of biopsy (Glenn and Thorbjarnarson 1964 *inter alia*).

The purpose of the present investigation was therefore to evaluate:
1/ the angiographic findings in inflammatory disease of the pancreas at various stages and forms.

- 2/ the diagnostic accuracy of angiography in carcinoma of the pancreas in a large series of patients with verified diagnosis.
- 3/ the causes of false diagnosis, either positive or negative, with particular reference to the differentiation between carcinoma and inflammatory disease.

Technique of examination

Since this study is mainly retrospective in nature and covers the period from 1959 to 1971, the examination technique has not been uniform. During the entire period, however, it has been the rule to examine both the coeliac and superior mesenteric arteries. The injections have been made either simultaneously or sequentially depending upon the circumstances; i.e. the anticipated findings, the degree of arteriosclerosis etc. "Superselective" catheterizations have sometimes been performed to obtain further information. They were seldom made during the first part of the period, but are now more often performed. During the entire period efforts have been made to aid diagnosis by using pharmacological agents such as epinephrine, norepinephrine, bradykinin, vasopressin, secretin and pancreozymin (Boijesen and Redman 1966, 1967, Boijesen and Göthlin). The filming procedure has been fairly constant. Roll film or cut film changer has been used and programmed to cover 15-20 seconds after contrast injection. The amount of contrast medium has been 30-40 ml of 76% concentration and the injection made by a pressure syringe. The importance of technical quality has been emphasized during the entire period and there has been a steady increase in the quality, but nevertheless a few examinations have failed in this respect and contributed to a false diagnosis. Comments on the technical quality have not been made if, despite poor technique, a correct diagnosis was made. Only in diagnostic failure has the contribution of the technical factors been evaluated.

INFLAMMATORY DISEASE OF THE PANCREAS (I, II and III)

Ödman (1959) observed hypervascularization, arterial displacement and venous lesions in chronic pancreatitis. Several reports have appeared since then considering hypervascularization to be characteristic of this disease (Baum et coll. 1965, Rösch and Bret 1965, Sammons et coll. 1967, Aakhus et coll. 1969, Reuter et coll. 1969, Bücheler et coll. 1971, Lechner and Pokieser 1971). Hypovascularization, however, also occurs, particularly in association with pseudocysts and even in disease without expansive lesions (Rösch and Bret 1965, Hernandez et coll. 1967, Reuter et coll. 1969, Bücheler et coll. 1971).

Displacement of arteries is frequently marked in the presence of an expansive lesion in the pancreas, but may also be caused by enlargement of the gland per se in chronic pancreatitis (Baum et coll. 1965, Rösch and Bret 1965, Nebesar and Pollard 1967, Sammons et coll. 1967, Reuter et coll. 1969, Taverniér et coll. 1969, Bücheler et coll. 1971, Lechner and Pokieser 1971).

Venous lesions when studied by splenoportography are common in pancreatitis (Anacker et coll. 1963, Rösch 1965), but when studied by arteriography the observed incidence is usually low (Reuter et coll. 1969, Bücheler et coll. 1971, Lechner and Pokieser 1971). Taverniér et coll. (1969), however, found venous involvement in more than half of their cases.

Stenotic changes of different morphological types in extrapancreatic arteries were frequently observed in chronic pancreatitis by Hernandez et coll. (1967). The findings have been confirmed by others but the incidence varies (Nebesar and Pollard 1967, Moskowitz et coll. 1968, Reuter et coll. 1969, Bücheler et coll. 1971, Lechner and Pokieser 1971).

Changes in intrapancreatic arteries consisting of alternating dilations and narrowings have also been noticed (Reuter et coll. 1969, Bücheler et coll. 1971, Lechner and Pokieser 1971). The latter changes have been considered characteristic of pancreatitis (Reuter et coll.).

Thus, opinions held on the vascular changes in angiography in pancreatitis are often contradictory. This is particularly true about the degree of vascularization. One cause of this disagreement may be that the evaluation of the vascularization depends to a great extent on the examination technique. Another cause may be that with few exceptions (Aakhus et coll. 1969, Reuter et coll. 1969), previous investigations lack the thorough clinical correlation by which the type and phase of inflammation may be deduced. This correlation is important since inflammatory disease of the pancreas occurs in chronic and acute forms and both forms may have a relapsing course in addition. Thorough clinical correlation was therefore considered necessary in this investigation in order to understand better the angiographic changes in the different forms and stages of pancreatitis.

Material

Eighty-seven patients with inflammatory disease of the pancreas were referred to the three groups; chronic, acute and relapsing pancreatitis, after considering etiological factors, symptoms, laboratory tests, operative and pathological findings and the duration of the disease.

The criteria for the chronic pancreatitis group were decreased exocrine pancreatic function, presence of calcifications in the pancreas or patho-anatomical findings consistent with the diagnosis. The group comprised 43 patients. Thirteen of them had more than one examination at varying intervals and were analysed separately (I). The fourteenth patient described in that paper was later referred to the group of relapsing pancreatitis, since despite numerous attacks and a decreased exocrine function at the time of the first part of the investigation, normal values for the exocrine function were revealed at a recent evaluation.

The criterium for acute pancreatitis was one attack of pancreatitis, verified by, for example, elevation of urinary or serum amylase and/or operative findings. The group comprised 28 patients.

The criterium for relapsing pancreatitis was two or more verified attacks. No effort was made to differentiate patients with chronic relapsing pancreatitis from those with acute recurring pancreatitis, but the patients did not fulfil the criteria for the group of chronic pancreatitis. The group comprised 16 patients.

Results

Arterial stenosis. Smooth, regular stenosis of arteries surrounding the pancreas was present in 84% of the patients with chronic, in 64% of those with acute and in 63% of those with relapsing pancreatitis. The stenosis was usually mild and occlusions were not observed. The length of the stenosis was varying, as was the appearance. It could appear like a concentric sleeve around the artery or be cone-shaped or be beaded in appearance resembling fibromuscular dysplasia. The stenosis was most often located in the splenic, gastroduodenal or common hepatic arteries. It was increased by injection of vasoconstrictive agents in some patients. The stenotic changes often increased and extended to more arteries with increased duration of disease. On the other hand the changes in a few patients had decreased or even disappeared at a repeat examination after operation. A short, concentric, often variable stenosis at the tip of the catheter was present in 21, 4 and 37% of the patients in the respective groups. This was interpreted as spasm induced by the catheter or the injected contrast medium. Stenosis of the coeliac artery was demonstrated in 16 patients and of the superior mesenteric artery in 9, in 7 of whom the lesions were combined.

Irregular pancreatic arteries. The lumen of the intrapancreatic arteries was slightly irregular in 56, 36 and 37% of the patients in the respective types of pancreatitis. It characteristically had a smoothly alternating width and therefore a beaded appearance. The changes occurred more frequently in patients with disease of long duration or many acute exacerbations. The changes were often associated with increased tortuosity of the vessels. Increased tortuosity of intrapancreatic arteries with or without lumen irregularities was

also common and was seen in 88, 78 and 63% of the patients, respectively.

Tortuous and irregular intestinal arteries were evident in 35, 25 and 25% of the patients of the different groups, respectively. The middle colic artery was usually involved. The changes were markedly progressive at repeat examinations in 5 patients with chronic pancreatitis.

Arterial aneurysm was demonstrated in 8 patients. An aneurysm was never demonstrated in a patient with calcifying chronic pancreatitis, but was otherwise evident in all types of inflammation. The aneurysms were located in the splenic artery in 5 patients and in the gastroduodenal artery in 3. Development of an aneurysm in the interval between two examinations was demonstrated in one patient. In another an aneurysm increased in size between the examinations.

Arterial displacement due to an abscess or a pseudocyst was demonstrated in 6, 8 and 3 patients in the respective groups. The displacement was usually marked and smoothly arciform. Displacement and stretching of the pancreatic arcades due to mere enlargement of the head of the pancreas was evident in 4 patients. The entire pancreatic vasculature and the gastroduodenal artery were markedly displaced to the left in another 4 patients with chronic pancreatitis and in one with relapsing pancreatitis. It was associated with marked retroperitoneal adhesions. The displacement had disappeared after resection of the tail of the pancreas in one patient at a second examination.

Venous lesions were evident in 60%, 53% and 44% of the patients, respectively. Occlusion of the veins was most frequent in chronic pancreatitis and compression in acute. The differentiation between occlusion and compression, however, was not always absolutely clear. Involvement of the splenic vein was usually noted, the superior mesenteric and portal veins generally only being affected in disease of long duration. There was an increase in the venous lesions when correlation was made to the duration of the disease in patients with chronic pancreatitis.

Vascularization. With the exception of calcifying chronic pancreatitis, when hypovascularization was the rule, no pattern of vascularization could be directly correlated to a particular type or phase of inflammation. In one patient with chronic pancreatitis enormous hypervascularization with arteriovenous shunting was demonstrated.

Pseudocyst or abscess was evident in 11 and 10 patients, respectively. Angiography proved to be the most reliable method for demonstrating pancreatic abscess, superior to survey films of the abdomen and barium studies. Angiographical differentiation between pseudocyst and abscess was not possible. Expansive lesions complicated the course of chronic and acute as well as relapsing pancreatitis. Displacement of the arteries was present in 17 of the 21 patients. In the absence of displacement the diagnosis was difficult. Stenotic arterial changes similar to those in uncomplicated inflammation were recorded in 20 of the patients and tortuous intrapancreatic arteries with lumen irregularities in 14. Venous lesions were demonstrated in 18 patients, in 2 of whom as the only indication of an expansive lesion. Changes in intestinal arteries were present in 10 patients. Thus arterial displacement was more common in the presence of an expansive lesion but otherwise the changes were similar to those in uncomplicated disease.

Discussion

Marked vascular changes were frequent in the present series and only 2 patients were regarded as being completely normal. Important differences between the various types of pancreatitis were not revealed. It should be pointed out that the high incidence of changes in the patients with acute pancreatitis may be due to the fact that they were usually examined because of a complicated or prolonged course of the disease. The stenotic changes of extrapancreatic arteries had different appearances but were always smooth. They were similar to those described by Hernandez et coll. (1967). These changes may be caused by postinflammatory fibrosis, but involvement of

the lymphatic system has also been suggested (Boijesen 1971). Accentuation of the stenosis by vasoconstrictive agents, the high incidence of spasm at the tip of the catheter and the tendency of the stenoses to decrease during remission may indicate, however, that they are not entirely of organic nature, but that spasm may be part of the process. The main rule was that the stenoses were more marked in patients with a long duration of the disease and with increasing number of attacks. Progress was often noted at repeat examinations.

In accordance with Reuter et coll. (1969) the irregular and tortuous intrapancreatic arteries were considered characteristic of pancreatitis. These changes were also progressive. Patho-anatomically, the changes consist of subintimal fibrosis and thickening of the media (Howard and Nedwick 1971).

The high incidence of arterial aneurysm is interesting. The often intense inflammatory process in surrounding tissues may cause necrosis of the arterial wall and an aneurysm may then develop. The tendency towards necrosis is less marked in calcifying chronic pancreatitis (Sarles et coll. 1965) and aneurysms were never observed among patients with this type of disease.

Marked fibrosis in retroperitoneal tissues is characteristic of chronic pancreatitis. This process caused marked displacement of the pancreas to the left in some patients. The displacement had sometimes increased at repeat examinations. Marked displacement of arteries, however, was usually associated with expansive lesions, such as pseudocysts or abscesses.

Venous lesions occurred more frequently than previously stated in arteriography. This was in accordance with the findings in splenoportography (Anacker et coll. 1963, Rösch 1965). Since there is a close relation between the large veins, particularly the splenic, and the pancreas, these lesions may be expected. The venous lesions were markedly progressive when correlated to the duration of the disease. The lesions were, however, sometimes reversible after operation, and this may be interpreted as being in favor of early

operative treatment.

It must be emphasized that the changes in the vessels surrounding the pancreas are unspecific. The arterial stenoses may be difficult to differentiate from primary vascular disease such as atheromatosis and the venous lesions may be caused by any expansive lesion in the retroperitoneal space, irrespective of a benign or malignant nature. The localization of the changes, to arteries and veins adjacent to the pancreas, however, may suggest the diagnosis of pancreatitis, but only in the presence of the characteristic changes in intrapancreatic arteries may the diagnosis be established with a fair degree of certainty.

CARCINOMA OF THE PANCREAS (IV and V)

A thorough description of the angiographic findings in carcinoma of the pancreas was first made by Lunderquist (1965). His results have been corroborated by other authors. Irregular encasement of arteries is the most common finding, but the frequency varies in different reports (Meaney and Buonocore 1965, Rösch and Bret 1965, Ludin et coll. 1966, Nebesar and Pollard 1967, Nusbaum et coll. 1967, Weissleder et coll. 1967, Bookstein et coll. 1969, Fredens et coll. 1969, Taverniér et coll. 1969, Lechner et coll. 1970, Bücheler et coll. 1971, Suzuki et coll. 1971). Encased larger arteries characteristically appear irregular and serrated, while the appearance in small arteries is more serpiginous (Bookstein et coll. 1969). Smooth regular stenotic changes also occur but usually in association with irregular encasement (Bookstein et coll. 1969, Reuter et coll. 1970).

Tumour vessels or tumour opacification is characteristic of tumours in many other locations, but in carcinoma of the pancreas tumour vessels are sparse and demonstrable only in examinations of high quality. The reported incidence of this finding is therefore generally low, but Lunderquist and Bookstein et coll. observed them in almost 60% of their cases. Displacement of the arteries does occur, but since a carcinoma infiltrates surrounding tissues rather than

displacing them, this is a rare observation (Lunderquist 1965, Olsson 1970). The incidence of venous lesions at arteriography is usually also low, but Taverniér et coll. and Buranasiri and Baum (1972) found involvement in 10 out of 12 and 46 out of 47 patients, respectively.

Thus most authors agree about the different types of vascular changes in carcinoma of the pancreas. They also agree that a diagnosis may be made. Disagreement, however, exists on the incidence of vascular changes and thus the diagnostic accuracy. It may be possible that only large, inoperable tumours cause changes which with present technical resources are demonstrable at angiography with any high degree of accuracy.

Material

Angiography was performed in 116 patients with carcinoma of the pancreas. The diagnosis was verified by post-mortem examination in 48, by surgery with biopsy in 41 and by surgery without biopsy in 25. In an additional 2 patients pathological verification was obtained by other means.

Results

Encasement of large arteries was evident in 54 patients. The splenic, gastroduodenal and common hepatic arteries were most frequently involved. Two or more arteries were encased in 23 patients. Encasement of large arteries was, in 44 instances, also associated with encasement of small arteries, while encasement of the latter alone was evident in 49. Thus encasement was evident in 103 patients (88%). In 13 patients no arterial encasement was demonstrated. Extension of the tumour into retroperitoneal structures and the root of the mesenterium as made evident by encasement of the coeliac artery and the main stem of the superior mesenteric artery was found in 10 and 9 patients, respectively.

Tumour vessels were observed in 75 patients (65%). They were the only indication of carcinoma in 6 patients. The tumour vessels

were usually sparse and tumour opacification of significant degree was not demonstrated.

Thus changes characteristic for tumours i.e. encasement of arteries and/or tumour vessels, were evident in 109 patients.

Changes which were pathological but not characteristic of carcinoma of the pancreas were, however, also common.

Smooth arterial stenoses of extrapancreatic arteries similar to those occurring in pancreatitis were present in 35 patients. Co-existent irregular encasement was demonstrated in all but 3 of them.

Irregular pancreatic arteries with alternating dilatations and narrowings of the lumen similar to the changes in pancreatitis were observed in 15 patients. The changes were usually located distal to a carcinoma of the head of the pancreas.

Displacement of arteries was evident in 31 patients. The gastroduodenal artery was displaced medially and kinked in 10 patients, and laterally with stretching of the pancreatic arcades in 7. Displacement of the entire pancreas and the gastroduodenal artery was evident in 9 patients with large tumours and extensive retroperitoneal growth and vast encasement of arteries.

Venous lesions were observed in 57 patients (49%). The incidence was particularly high in carcinoma of the body and tail of the pancreas. The splenic vein was most often involved and was usually occluded. The incidence was not that high in carcinoma of the head of the pancreas and the involvement was then more often by compression.

Other findings such as tortuous arteries and abnormalities of vascularization were unspecific and of little help in the diagnosis.

Discussion

The diagnosis of carcinoma of the pancreas may be made by demonstration of arterial encasement and of tumour vessels only. The diagnosis may, however, be supported by unspecific findings such as venous lesions and arterial displacement. In our series irregu-

lar encasement of arteries was present in 103 of the 116 patients. The incidence is about the same as previously stated (Lunderquist 1965, Bookstein et coll. 1969, Taverniér et coll. 1969, Lechner et coll. 1970, Bücheler et coll. 1971). Encasement of small pancreatic arteries was more common than encasement of large arteries, but in 23 patients two or more arteries were encased indicating large tumours. The incidence of large arterial involvement was particularly high in patients with carcinoma of the tail of the pancreas and in all these the splenic artery was encased. This high incidence is probably due to the fact that tumours of this part of the pancreas are usually large by the time of diagnosis (Miller et coll. 1951). Encasement of the coeliac, left gastric, renal and superior mesenteric arteries may be interpreted as indicating extension of the growth to the retroperitoneal structures and the root of the mesenterium and thus inoperability.

Tumour vessels, though small and sparse were demonstrated in 75 patients. The incidence is about the same as reported by Lunderquist and Bookstein et coll. To be able to demonstrate this delicate pathological vasculature, high technical quality is necessary and by improvement of our technique it will be demonstrated more often.

Smooth arterial stenosis and irregular pancreatic arteries, changes which are common in pancreatitis, were demonstrated in 35 and 15 patients respectively. In most patients concomitant irregular encasement of tumour vessels, were also evident and the correct diagnosis therefore obvious, but differentiation was sometimes difficult. The findings may be explained by the fact that inflammatory changes are common in the periphery of a carcinoma (Gambill 1971).

Displacement of arteries was evident in 31 patients. The finding, however, is only an indication of an expansive lesion and therefore not characteristic of carcinoma. Displacement is moreover difficult to evaluate, because of the great normal variations in vascular anatomy, unless it is evident in conjunction with arte-

rial encasement. The marked displacement of the pancreatic vasculature to the left demonstrated in 9 patients was interpreted as indicating retroperitoneal invasion. A similar type of displacement may be demonstrated in chronic pancreatitis and is then caused by retroperitoneal adhesions (Boijesen and Tylén 1972).

Venous lesions were demonstrated in 49% of the patients in this material. This incidence is considerably higher than that usually observed. From investigations by splenoportography in pancreatic disease, however, it is well known that venous lesions are common in carcinoma (Anacker et coll. 1963, Rösch 1965). The reported low incidence of venous lesions in arteriography must therefore be due to technical factors. Buranasiri and Baum (1972) focused their interest on the veins and found venous involvement in 97% of their patients. It must, however, be stressed that venous lesions are unspecific and common also in pancreatitis.

DIFFERENTIAL DIAGNOSIS AND DIAGNOSTIC ACCURACY (III, IV and V)

The angiographic findings in carcinoma of the pancreas and in pancreatitis are characteristic. Due to the similarity of the changes, however, differential diagnostic difficulties may arise. This was anticipated by Lunderquist (1965) and has since been sustained by others (Rösch and Bret 1965, Sammons et coll. 1967, Nebesar and Pollard 1967, Moskowitz et coll. 1968, Fredens et coll. 1969, Benkö 1970, Lechner et coll. 1970, Bücheler et coll. 1971). With increasing familiarity with the angiographic changes in the two diseases, however, differential diagnostic difficulties seldom occur (Bookstein et coll. 1969, Reuter et coll. 1969, 1970). In the present investigation the diagnostic difficulties in carcinoma of the pancreas were evaluated by analysis of the angiographic examinations in which an incorrect diagnosis had been made. Analysis of the accuracy of the angiographic diagnosis of pancreatitis was not attempted since verification of the diagnosis could not be provided in all cases. Only patients in whom the differentiation between carcinoma and pancreatitis was difficult were particularly evaluated.

Material

Among 116 patients with verified carcinoma of the pancreas, a correct preoperative diagnosis was made in 79 (68%). In the remaining patients the diagnosis was pancreatitis in 11, postoperative changes in 3, atheromatosis in 2 and in 2 patients arterial stenosis was observed, but not associated with carcinoma. No pathological changes with reference to the pancreas were reported in 19 cases. An additional 2 patients who had repeat examinations were initially diagnosed as having pancreatitis. Ultimately, however, the correct diagnosis was made and the patients therefore considered to be correctly diagnosed. One more patient with diagnosis of pancreatitis, reported in paper nr IV, was later excluded since the verification was considered insufficient.

Moreover, angiographic diagnosis of carcinoma of the pancreas was incorrectly made in 18 patients, in whom the operative findings were pancreatitis in 5, stones in the choledochal duct in one and stenosis of the papilla of Vater in one. A normal pancreas was revealed at operation in 8 patients, while no operation was performed in 3. In the latter patients, no subsequent signs of pancreatic carcinoma have developed.

Results

Preoperatively, the pancreatic carcinoma were not diagnosed in 37 patients. A retrospective diagnosis was possible in 30 of these (Table I). The analysis of the 11 patients with an incorrect diagnosis of pancreatitis disclosed changes characteristic of carcinoma in 9. Irregular encasement and/or tumour vessels were evident in 5, one of whom had two examinations. Poor technique may have contributed to the incorrect diagnosis in 2 cases and concomitant inflammatory vascular changes in one of these. In an additional 2 patients, in whom changes suggestive of carcinoma were evident, poor examination technique definitely rendered the diagnosis impossible.

Table I.

CHANGES AT RETROSPECTIVE ANALYSIS OF 37 PATIENTS WITH CARCINOMA OF THE PANCREAS WITH INCORRECT PREOPERATIVE DIAGNOSIS.

Preoperative diagnosis	Retrospective diagnosis possible		Tumour changes not demonstrable	
Pancreatitis	11	Encasement	5	
		Displacement+ encasement	2	
		Poor technique	2	9 2
Postoperative changes	3	Encasement and/or tumour vessels	3	-
Atheromatosis	2	Encasement	2	-
Arterial stenosis	2	Encasement	2	-
Normal findings	19	Encasement	12	
		Tumour vessels alone	2	14 5 ^x
Total	37		30	

^xpoor technique of examination in one patient

Expansive lesions of the pancreas contributed directly to the false interpretation of the findings in 2 patients. The patients had long histories of pancreatitis and one of them had pancreatic calcifications in addition. At operation carcinomas with cystic degeneration were disclosed. Retrospectively, encasement of small pancreatic artery branches was demonstrated in both.

Angiographic diagnosis of pancreatitis was made in another 2 patients, one of whom had had pancreatitis for several years. At angiography a pseudocyst was diagnosed. Operation confirmed this diagnosis, but in addition a carcinoma was revealed. The other patient with changes compatible with pancreatitis had a small removable carcinoma of the

head of the pancreas although the angiographic changes were located in the body and tail . In these 2 patients even retrospective analysis disclosed no evidence of carcinoma.

Although angiographic changes characteristic of tumours were evident in an additional 7 patients, the changes were interpreted as being due to previous operations in 3, atheromatosis in 2 and irregular stenosis of arteries in the remaining 2. The latter 2 patients were examined during the early years of angiography.

Normal findings in the pancreas were reported in 19 patients with carcinoma. The correct retrospective diagnosis was made in 14 of these. The tumours were large in 8 instances and small in 6. Encasement of large arteries, tumour vessels and venous lesions were demonstrated in 3 patients, while small artery encasement was evident in 9. Tumour vessels were, in 2 patients, the sole pathological finding.

Retrospective diagnosis was not possible in 7 patients, 2 of whom were mentioned above and diagnosed as having pancreatitis. The findings were sparse in 2 other patients with small tumours; some hypervascularization and a few tortuous vessels, respectively. The tumours were large in the remaining 3 patients. In spite of this, the findings were not characteristic of carcinoma. In one of the latter patients, however, the technical quality was poor, since the catheter recoiled to the aorta and the contrast filling of the arteries was therefore poor.

A false diagnosis of carcinoma of the pancreas was made in 18 patients. Tortuous and irregular arteries, tumour vessels or tumour opacification and vascular displacement were the findings which were considered diagnostic. Operation was performed in 11 patients. Pancreatitis was revealed in 5, in one of whom induration was present in the entire gland. At retrospective analysis this corresponded well to arterial changes, characteristic of pancreatitis, involving the entire gland. The other 4 patients with pancreatitis had circumscribed lesions in the head of the pancreas, in one patient in association with a pseudocyst. Retrospectively the changes

in these 4 patients were marked and localized, and malignancy was therefore again diagnosed. Marked, localized, arterial irregularities were evident in an additional patient in whom carcinoma was suggested. At operation a completely normal gland was revealed. In the remaining patients the vascular changes, preoperatively reported as characteristic of carcinoma, were at the retrospective analysis regarded as being within normal limits.

The incidence of false diagnosis of pancreatitis was not possible to evaluate, since verification was seldom provided. In some patients, however, with false positive diagnosis, retroperitoneal tumours of low vascularity such as reticulum cell sarcoma or lymph node metastasis were revealed at operation. Moreover, pancreatitis was sometimes suggested based on the demonstration of arterial aneurysms or stenotic changes of extrapancreatic arteries. In patients operated upon, however, the pancreas was without pathological changes and the cause of the changes was therefore probably primary vascular disease. Coeliac artery stenosis with wide and tortuous collaterals sometimes caused marked hypervascularization of the pancreas. The finding had probably nothing to do with inflammatory disease of the pancreas, but operative verification was not provided.

Discussion

It must be realised that the technical quality of the examination and the ability to differentiate pathological changes from normal variations are the basic requirements for obtaining a high degree of accuracy in the diagnosis of carcinoma of the pancreas. The former problems may be solved in many ways, but the latter problem may only be solved by personal experience of pancreatic angiography. Since this study comprises patients examined during the period from the start of selective visceral angiography up to recent date, we have gradually gained increasing experience. Therefore many false diagnoses of yesterday may have been avoided with the experience of today. Thus false positive diagnosis of carcinoma was made in

12 patients who at retrospective analysis were considered to have normal anatomical variations. Moreover, changes characteristic of carcinoma were observed and reported in 7 patients, but a false diagnosis was made. No pathological changes were reported in an additional 14 patients in whom tumour changes were demonstrated retrospectively. The changes were extensive in 3. In these patients, the false diagnosis would have been avoided with more experience. Personal experience is also of utmost importance when evaluating pathological changes. Carcinoma of the pancreas and pancreatitis cause characteristic changes, but these may be similar and false interpretation may result. In this retrospective study, differentiation was usually possible. Exceptions were 2 patients in whom changes diagnostic of carcinoma were not at all demonstrable and pancreatitis was therefore diagnosed, and 4 patients in whom circumscribed marked arterial irregularities were evident. An incorrect diagnosis of carcinoma was made in these latter patients by adhering to the rule that carcinoma causes localized arterial changes, while changes in pancreatitis are generalized (Reuter et coll. 1970). Changes caused by carcinoma together with inflammatory changes appeared in 15 patients in the present series. This constitutes a real difficulty. The inflammatory changes, however, were located distal to a carcinoma of the head of the pancreas and the finding of localized inflammatory changes should therefore always raise suspicion of carcinoma and the examination must continue until a tumour can be ruled out.

Carcinoma of the pancreas may also develop as a complication to chronic pancreatitis, particularly in the presence of calcifications (Paulino-Netto et coll. 1960, Lundh and Nordenstam 1970, Robinson et coll. 1970). Under such circumstances the differential difficulties are at a peak. This occurred in 3 patients in the present series, in all of whom expansive lesions, probably pseudocysts were diagnosed. Development of pseudocysts in carcinoma of the pancreas seldom occurs (Buck and Fletcher 1972), but the angiographer should be aware of the possibility in order not to overlook a carcinoma.

It may be concluded from this part of the study that the differentiation between carcinoma of the pancreas and pancreatitis may usually be made by following the main rule that stenotic arterial changes in pancreatitis are smooth and therefore different from the irregular encasement of pancreatic carcinoma. Tumour vessels, moreover, are much more irregular and deranged than the smooth alternating lumen variations of pancreatitis. Furthermore the changes in pancreatitis are more generalized than those in carcinoma unless the tumour is very large, in which case, however, arterial encasement is usually extensive. Differential diagnostic difficulties may arise e.g. in the presence of circumscribed pancreatitis or expansive lesions. In the presence of strictly localized changes it may be better to make a false positive diagnosis in order to occasionally find a tumour which is amenable to radical surgery. The best way, however, may be to repeat the examination after a suitable time interval.

The greatest problem in pancreatic angiography is the group of 7 patients, 4 with large tumours, in whom diagnosis was impossible even in retrospect. It is hoped that further improvement of our technical equipment and/or use of other pharmacological agents will permit diagnosis also in these patients.

General summary and conclusions

Retrospective analysis of 87 patients with chronic, acute and relapsing pancreatitis disclosed high incidence of vascular changes; only 2 patients had completely normal examinations, Smooth, regular stenoses of varying lengths in extrapancreatic arteries, smooth lumen irregularities and increased tortuosity of intrapancreatic arteries, and lesions of the large veins were the most common findings. Arterial aneurysms and expansive lesions, abscesses or pseudocysts, moreover often complicated the disease. The vascular changes were similar in different types of inflammation, but were more marked in complicated disease and disease of long duration. In patients examined more than once the changes were often progressive.

In pancreatic carcinoma retrospective diagnosis was made in 109 of the 116 patients (94%). The most frequent pathological findings were irregular encasement of arteries and tumour vessels. Moreover venous lesions were demonstrated in about half of the patients. Correct preoperative diagnosis of carcinoma was made in 79 of the 116 patients (68%). In the remaining, an incorrect diagnosis, such as pancreatitis, postoperative changes, arteriosclerosis was made. Incorrect positive diagnosis of carcinoma was made in 18 patients in addition. Retrospective analysis of these incorrectly diagnosed patients permitted correct diagnosis of the tumour in all but 7; moreover tumours could be ruled out in 13 of the 18 with incorrect positive diagnosis. The remaining 5 patients presented markedly irregular arteries within a small area, corresponding to circumscribed pancreatitis in 4 patients.

It may thus be concluded from this study that arteries affected by carcinoma characteristically appear irregularly stenosed. The changes are usually localized, unless the tumour is large, in which case the vascular changes may be marked. The arterial involvement in inflammatory disease, on the other hand, has a smooth regular appearance. The involvement is more often generalized and several extrapancreatic arteries may then be affected.

Tumour vessels, being newly formed, are markedly deranged and appear different from the smooth regular lumen variations seen in inflammatory disease. Moreover, tumour vessels usually occur within the usually small area corresponding to the tumour, while inflammatory changes are more dissiminated.

The displacement of vessels in pancreatitis is smooth and arch-shaped but in carcinoma it is usually less marked and more abrupt and irregular. Venous lesions occur frequently in carcinoma as well as in inflammatory disease and do not permit differentiation. Difficulties in differentiation may appear when changes caused by inflammatory and malignant disease occur simultaneously and in the presence of localized arterial irregularities, corresponding to circumscribed pancreatitis. With increasing experience, however,

the difficulties seldom arise.

It should be realized that there can be tumours, even large ones, which with present technique and skill may not be diagnosed.

Angiography, however, affords great help in the diagnosis of pancreatic disease.

REFERENCES

- AAKHUS T., HOFSLI M. and VESTAD E.: Angiography in acute pancreatitis. *Acta Radiol.* 8 (1969), 119.
- ANACKER H., LINDEN G. und HUMPERT R.: Die chronische Pancreaserkrankungen im Splenoportogramm. *Fortschr. Röntgenstr.* 99 (1963), 129.
- BAUM S., ROY R., FINKELSTEIN A.K. and BLAKEMORE W.S.: Clinical application of selective coeliac and superior mesenteric angiography. *Radiol.* 84 (1965), 279.
- BEALL S.M., DYER G.A. and STEPHENSON H.E.: Disappointments in the management of patients with malignancy of pancreas, duodenum and common bile duct. *Arch. Surg.* 101 (1970), 461.
- BENKÖ G.: Problems of differential diagnosis in angiography of the pancreas. *Radiol. clin.* 39 (1970), 334.
- BOIJSSEN E.: Pancreatic angiography: in Abrams H.L. *Angiography*. Little, Brown and Company 1971, Boston, Mass.
- BOIJSSEN E. and GÖTHLIN J.: Vasopressin in angiography of abdominal arteries. To be published.
- BOIJSSEN E. and REDMAN H.C.: Effect of Bradykinin on coeliac and superior mesenteric angiography. *Invest. Radiol.* 1 (1966), 422.
- BOIJSSEN E. and REDMAN H.C.: Effect of epinephrine on coeliac and superior mesenteric angiography. *Invest. Radiol.* 2 (1967), 184.
- BOIJSSEN E. and TYLÉN U.: Vascular changes in chronic pancreatitis. *Acta Radiol. (Diagn.)* 12 (1972), 34.
- BOOKSTEIN J.J., REUTER S.R. and MARTEL W.: Angiographic evaluation of pancreatic carcinoma. *Radiology* 93 (1969), 757.
- BOURKE J.B., BROWN C.L., RITCHIE H.D. and SWANN J.C.: Exocrine pancreatic function studies, duodenal cytology and hypotonic duodenography in the diagnosis of surgical jaundice. *Lancet* 1 (1972), 605.
- BUCK B.A. and FLETCHER W.S.: Carcinoma associated with pancreatic cyst. *Surg. Gyn. Obst.* 134 (1972), 44.

- BURANASIRI S. and BAUM S.: The significance of the venous phase of celiac and superior mesenteric arteriography in evaluating pancreatic carcinoma. *Radiology* 102 (1972), 11.
- BÜCHELER E., BOLDT I., FROMMHOLDT H. und KÄUFER C.: Die angiographische Diagnostik der Pancreastumoren und der Pancreatitis. *Fortschr. Röntgenstr.* 115 (1971), 726.
- BÖTTGER E., OCHSENSCHLÄGER A., ASMAR F. und HASSELBACH D.: Zum Aussagewert der Hypotonen Duodenographie in der Diagnostik und Differentialdiagnostik der Duodenal- und Pancreas-Erkrankungen. *Fortschr. Röntgenstr.* 116 (1972), 509.
- DESGREZ A., BISMUTH H., TESTAS , REGENSBERG C., BOK B. et LEMORT J-P.: Pancréas, scintigraphie et soustraction électronique. *Nouv. Presse Med.* 1 (1972), 1003.
- DOUBILET H., POPPEL M.H. and MULHOLLAND J.H.: Pancreatography, Technic, principles and observations. *Radiology* 65 (1955), 325.
- DREILING D.A.: The early diagnosis of pancreatic cancer. *Scand. J. Gastroent. Suppl.* 6 (1970), 115.
- FEDUSKA N.J., DENT T.L. and LINDENAUER S.M.: Results of palliative operations for carcinoma of the pancreas. *Arch. Surg.* 103 (1971), 330.
- FREDENS M., EGEBLAD M. and HOLST-NIELSEN F.: The value of selective angiography in the diagnosis of tumors in pancreas and liver. *Radiology* 93 (1969), 765.
- FRIMAN-DAHL J.: Radiology in tumours of the pancreas. *Clin. Radiol.* 12 (1961), 73.
- GAMBILL E.E.: Pancreatitis associated with pancreatic carcinoma: a study of 26 cases. *Mayo Clin. Proc.* 46 (1971), 174.
- GLENN F. and THORBJARNARSON B.: Carcinoma of the pancreas. *Ann. Surg.* 159 (1964), 945.
- GOLDSTEIN H. and VENTZKE L.E.: Value of exfoliative cytology in pancreatic cancer. *GUT* 9 (1968), 316.

- GUIÉN Cl., PIETRI H. et SURDON P.: Comparaison statistique entre l'angiographie sélective et la tomographie dans les cancer du pancreas et les pancréatites chroniques. Arch. Mal. Appar. Dig. 59 (1970), 384.
- HERNANDEZ Cl., ECARLAT B. et BISMUTH V.: L'arteriographie des affections pancréatiques. J. Radiol. 48 (1967), 327.
- HOWARD J.M. and NEDWICH A.: Correlations of the histologic observations and operative findings in patients with chronic pancreatitis. Surg. Gyn. Obst. 132 (1971), 387.
- HOWARD J.M. and SHORT W.F.: An evaluation of pancreatography in suspected pancreatic disease. Surg. Gyn. Obst. 129 (1969), 319.
- KRAIN L.S.: The rising incidence of carcinoma of the pancreas. An epidermologic appraisal. Am. J. Gastroenterol. 54 (1970), 500.
- KRÖNERT E. und WOLF F.: Der gegenwärtige Stand der Pancreaszintigraphie. Leber Magen Darm 3 (1972), 82.
- LECHNER G. und POKIESER H.: Ergebnisse angiographischer Untersuchungen bei pancreatitis. Fortschr. Röntgenstr. 114 (1971), 49.
- LECHNER G., POKIESER H., ZAUNBAUER W. und BRÜCKE P.: Zur angiographischen Diagnose des Pancreaskarzinoms. Fortschr. Röntgenstr. 113 (1970), 340.
- LUDIN H., FAHRLÄNDER H.J. und MAURER W.: Arteriographische Diagnostik im Karzinomen des Pankreaskörpers und -schwanzes. Schweiz. Med. Wochenschr. 96 (1966), 871.
- LUNDERQUIST A.: Angiography in carcinoma of the pancreas. Acta Radiol. (1965) Suppl. No. 235.
- LUNDH G.: Pancreatic exocrine function in neoplastic and inflammatory disease: a reliable and simple test. Gastroenterology 42 (1962), 275.
- LUNDH G. and NORDENSTAM H.: Pancreas calcification and pancreas cancer. Acta Chir. Scand. 136 (1970), 493.
- McCARTHY D., BROWN P., MELMED R.N., AGNEW J.E. and BOUCHIER I.A.D.: Se-Selenomethionine scanning in the diagnosis of tumours of the pancreas and adjacent viscera: The use of the test and its impact on survival. GUT 13 (1972), 75.

- MEANEY Th. F. and BOUONOCORE E.: Arteriographic manifestations of pancreatic neoplasms. *Amer. J. Roentgenol.* 95 (1965), 720.
- MILLER J.R., BAGGENSTOSS A.H. and COMFORT M.W.: Carcinoma of the pancreas: effect of histological type and grade of malignancy on its behaviour. *Cancer* 4 (1951), 233.
- MOSKOWITZ H., CHAIT A. and MELLINE H.Z.: "Tumour encasement" of the coeliac axis due to chronic pancreatitis. *Amer. J. Roentgenol.* 104 (1968), 641.
- National Board of Health and Welfare. The Cancer Registry. Cancer Incidence in Sweden 1959 - 1965. Göteborgs Offsettryckeri AB, Stockholm 1972.
- NEBESAR R.A. and POLLARD J.J.: A critical evaluation of selective celiac and superior mesenteric angiography in the diagnosis of pancreatic disease, particularly malignant tumor, facts and artefacts. *Radiology* 89 (1967), 1017.
- NUSBAUM M., BAUM S., KUZODA K., BLAKEMORE W.: Selective mesenteric arteriography in the diagnosis of pancreatic lesions. *Amer. J. Gastroenterol.* 48 (1967), 421.
- OI I., KOBAYASHI S. and KONDO T.: Endoscopic pancreatocholangiography. *Endoscopy* 2 (1970), 103.
- OLSSON O.: Angiography in tumours of the pancreas. In: *Modern trends in diagnostic radiology*. Ed. J.N. McLaren. Butterworths 1970.
- PAULINO-NETTO A., DREILING D.A. and BORONOFKY I.D.: The relationship between pancreatic calcification and cancer of the pancreas. *Ann. Surg.* 151 (1960), 530.
- PEREZ C.A., POWERS W.E., HOLTZ S. and SPJUT H.J.: Roentgenologic-pathologic correlation of resectable carcinoma of the pancreatico-duodenal region. *Amer. J. Roentgenol.* 94 (1965), 438.
- POPE N.A. and FISH J.C.: Palliative surgery for carcinoma of the pancreas. *Amer. J. Surg.* 121 (1971), 271.
- REUTER S.R., REDMAN H.C. and BOOKSTEIN J.J.: Differential problems in the angiographic diagnosis of carcinoma of the pancreas. *Radiology* 96 (1970), 93.

- REUTER S.R., REDMAN H.C. and JOSEPH R.R.: Angiographic findings in pancreatitis. *Amer. J. Roentgenol.* 107 (1969), 56.
- ROBINSON A., SCOTT J. and ROSENFELD D.D.: The occurrence of carcinoma of the pancreas in chronic pancreatitis. *Radiology* 94 (1970), 289.
- RUBINSTEIN Z.J., BANK S., MARKS I.N. and PSILLOS C.: Hypotonic duodenography in chronic pancreatitis. *Brit. J. Radiol.* 44 (1971), 142.
- RÖSCH J.: Die Splenoportographie in der Diagnostik der Pankreas-erkrankungen. *Radiology* 5 (1965), 274.
- RÖSCH J.: Roentgenology of the spleen and pancreas. Charles C. Thomas. Springfield, Ill., U.S.A. 1967.
- RÖSCH J. and BRET J.: Angiography of the pancreas. *Amer. J. Roentgenol.* 94 (1965), 182.
- SALIK J.O.: Pancreatic carcinoma and its early roentgenologic recognition. *Amer. J. Roentgenol.* 86 (1961), 1.
- SAMMONS B.P., NEAL M.P., ARMSTRONG R.H. and HAGER H.D.: Ten years experience with celiac and upper abdominal superior mesenteric arteriography. *Amer. J. Roentgenol.* 101 (1967), 345.
- SARLES H., SARLES J.C., CAMATTE R., MURATOIRE R., GAINI M., GUIÉN C., PASTOR J. and LEROY F.: Observations in 205 confirmed cases of acute pancreatitis, recurring pancreatitis and chronic pancreatitis. *GUT* 6 (1965), 545.
- SELDINGER S.J.: Percutaneous transhepatic cholangiography. *Acta Radiol.* (1966) Suppl. No. 253.
- SUZUKI T., KAWEBE K., NAKAYASU A., TAKEDA H., KOBAYASHI K., KABUTO N. and HONJO I.: Selective arteriography in cancer of the pancreas at a resectable stage. *Amer. J. Surg.* 122 (1971), 402.
- TAKAGI K., IKEDA S., NAKAYAWA Y., KAMAKURA K., MANYAMA M., SOMEYA N., TAKEDA T. and TAKAHASHI T. and KISS T.: Endoscopic cannulation of the ampulla of Vater. *Endoscopy* 2 (1970), 107.
- TAVERNIER J., DELORME G., LAFITTE J., TESSIER J. et BELLET M.: Apports de l'angiographie coeliaque et mésentérique à la radiographie pancréatique. *J. Radiol.* 50 (1969), 867.

- TRAPNELL J.: The operative diagnosis of carcinoma of the pancreas.
Brit. J. Surg. 58 (1971), 849.
- WEISS H.D., ANACKER H. und WIESNER W.: Die Technik der Duodeno-
skopie mit retrograder Pancreatiko- und Cholangiographie.
Fortschr. Röntgenstr. 116 (1972), 517.
- WEISSLEDER W., RÄDEKER V., NIEMANN H. und EMMERICH J.: Pancreas
Diagnostik durch selektive Angiographie. Röntgenblätter
20 (1967), 501.
- WIECHEL K.L.: Transhepatic cholangiography. Acta Chir. Scand.
(1964) Suppl. No. 330.
- ÖDMAN P.: Percutaneous selective angiography of the coeliac ar-
tery. Acta Radiol. (1958) Suppl. 159.

STUDENTLITTERATUR
LUND SWEDEN